REMARKS

Responsive to the Office Action mailed October 1, 2004, with an extension of time of THREE MONTHS, the request for which is filed herewith with an authorization to debit deposit account 11-0600, the present paper is timely filed on or before **April 1, 2004**. By the present paper, claims 19 and 99 – 101 are cancelled and claim 1 is amended. Accordingly, claims 1 to 18, 20 - 98 and 102 to 112 are in the application. Entry of the amendments and reconsideration of the application are respectfully requested.

The Claim Amendments

Claim 1 is amended to point-out with even greater particularity that the gastric retention vehicle claimed therein is characterized by the functional limitation that it expand about three fold within about 15 minutes of contacting simulated gastric fluid. Support for the amendment can be found, for example, in claims 1 and 19 as filed.

Claim 19 is presently cancelled.

Double Patenting Rejections

[01] Claims 1-35 and 35 - 82 were provisionally rejected on the basis of obviousness-type non-statutory double patenting in view of commonly-owned United States patent 6,476,006 and published United States Patent Applications 10/420,403 (U.S. 2003/0158154) and 10/196,766 (u.s. 2003/0158154). Claims 1 - 33 were provisionally rejected on the basis of obviousness-type non-statutory double patenting in view of commonly owned United States patent Application 10/026,573 (U.S. 2002/0147,208).

[02] Concerning United States Patent 6,476,006, Applicants respectfully submit that the contemporaneously filed terminal disclaimer removes any basis for the rejection that may have existed. The fully executed disclaimer will follow in due course. Accordingly, Applicants respectfully submit that the rejection should be withdrawn.

[03] Concerning United States Patent Application 10/420,403, Applicants respectfully submit that the contemporaneously filed Terminal Disclaimer obviates any basis for the provisional rejection that may have existed and, accordingly, that the rejection should be withdrawn. The fully executed disclaimer will follow in due course.

[04] Concerning U.S.S.N. 10/196,766, claims 1 - 33 of the published application are drawn to a dosage form for sequential delivery of a bisphosphonate and a vitamin D derivative. The Office alleges that claims 1-3 and 35-82 of the instant invention are obvious

over claims 1-33 of the '766 application. Applicants respectfully submit that the contemporaneously filed terminal disclaimer obviates any grounds for the rejection that may have existed and, accordingly, that the rejection should be withdrawn. The fully executed disclaimer will follow in due course.

[05] Concerning United States Patent Application 10/026,573, Applicants respectfully submit that the contemporaneously filed Terminal Disclaimer removes any basis for the non-statutory provisional rejection that may have existed and that the rejection should be withdrawn. The fully executed disclaimer will follow in due course.

Claim Rejections Under 35 U.S.C. § 102

[06] Claims 1 -7, 9 - 14, 19 - 31, 35 - 38, 40 -50, 52 - 82, and 97 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by William J. Curatolo et al., Published United States Patent Application 09/742,785, published as 2002/0006443 (Curatolo '443). Because Curatolo '443 does not teach all of the elements (limitations) of Applicants' claims, arranged as arranged in Applicants' claims, Applicants respectfully traverse.

[07] Concerning claim 1, Applicants respectfully submit that, contrary to the assertion in the Office Action, "contacting gastric fluid" is not a statement of future intended use, rather it is part of an express functional limitation of the gastric retention vehicle of claim 1: "wherein the volume of the composition increases about three-fold within about 15 minutes of contacting gastric fluid". Moreover, even *if* the words "contacting gastric fluid" *were* a statement of intended use, this statement cannot be completely ignored. M.P.E.P. § 2111.02. Applicants respectfully submit that the Office has failed to consider all of the limitations of claim 1 and that, when all limitations are considered, in particular the limitation "wherein the volume of the composition increases about three-fold within about 15 minutes of contacting gastric fluid", it is plain that Curatolo '443 does not teach all of the limitations of claim 1. Accordingly, Applicants respectfully submit that the rejection of claim 1 should be withdrawn. *See* M.P.E.P § 2131 (a claim is anticipated only if each and every element as set forth in the claim is expressly or inherently described in a single prior art reference).

[08] Applicants respectfully submit that the present amendments to claim 1 further distinguish the present invention over Curatolo '443.

[09] Concerning claims 2 - 7, 9 - 14, and 19 - 21, these claims depend from claim 1 and, *per force*, further limit the novel subject matter of claim 1. Accordingly, Applicants respectfully submit that Curatolo '443 can not teach all of the limitations of these claims and that the rejection of claims 2 - 7, 9 - 14, and 19 - 21 should therefore be withdrawn.

[10] Turning now to claim 22, at the very least this claim includes a limitation to physical degradation ("break-up") of the dosage form not taught or suggested by Curatolo '443. For this reason alone, Applicants respectfully submit that the rejection should be withdrawn.

[11] Furthermore, any cellulose derivatives of Curatolo '443 that might be capable of functioning as superdisintegrants in the instant invention function as "concentration enhancing polymers" in Curatolo '443. These "concentration enhancing polymers" can be administered completely separately from the active pharmaceutical ingredient". Clearly, these "concentration enhancing polymers do not perform the function of the superdisintegrants in the instant invention. Applicants respectfully submit that mere recitation of an element in a prior art reference is not necessarily sufficient to anticipate. Rather, that particular element must function or be capable of functioning in the prior-art device or composition in the way in which that element functions in the allegedly anticipated device or composition. *See Minnesota Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1569 (Fed. Cir. 1992). The cellulose derivatives of the present invention are part of and function only as part of the dosage form and clearly function in a different way than the "concentration enhancing polymers" of Curatolo '443. For this additional reason, Applicants respectfully submit that Curatolo '443 does not anticipate Applicants' claim 22, or, *per force*, any of claims 23 - 31 that depend from claim 22. and that the rejection of claim 22 - 31 should be withdrawn.

[12] Turning now to claim 40, claim 40 requires, *inter alia*, that the gastric retention vehicle provide a solid matrix in which the therapeutic agent is dispersed and expand on contact with gastric fluid. Moreover, as discussed above in relation to claim 22, the cellulose derivatives disclosed in Curatolo '443 function as concentration enhancing agents and do not function in the manner in which they function in Applicants' invention. Accordingly, Applicants respectfully submit that the rejection of claim 40 should be withdrawn

[13] Concerning claims 41 - 50, these claims depend from claim 40. Because claim 40 is not anticipated, dependent claims 41 - 50 are likewise not anticipated and, accordingly, Applicants respectfully submit that the rejection should be withdrawn.

[14] Turning now to claim 52, claim 52 describes with particularity a dosage form comprising a gastric retention vehicle that must include three elements and that has dispersed in it first and second particles which second particles must have a coating that meets certain functional limitations. Applicants respectfully submit that Curatolo '443 does not expressly or inherently teach all of the limitations of Applicants' claim 52 and that the rejection should

be withdrawn.

[15] Turning now to claim 53, claim 53 describes with particularity a dosage form comprising, *inter alia*, a gastric retention vehicle that provides a matrix for first and second particles each of which first and second particles have coatings that must meet particular functional limitations concerning permeability and dissolution. Applicants respectfully submit that Curatolo '443 does not suggest, let alone teach, any of these limitations. Accordingly, Applicants respectfully submit that the rejection of claim 53 should be withdrawn.

[16] Turning now to claim 54, claim 54 describes with particularity a dosage form having a compacted reservoir containing a therapeutic agent. The reservoir is embedded in a shell, made by compaction that includes a hydrogel, a superdisintegrant, and tannic acid. Applicants respectfully submit that Curatolo '443 does not even suggest, let alone teach, a dosage form that meets all of the limitations of the core-shell dosage form of claim 54. Accordingly, Applicants respectfully submit that the rejection of claim 54 should be withdrawn.

[17] Concerning claims 55 - 66, these claims depend from claim 54. Because claim 54 is not anticipated, claims 55 -56 depending therefrom are also not anticipated. Applicants respectfully submit that the rejection of claim 55 - 66 should be withdrawn.

[18] Turning now to claim 67, claim 67 describes with particularity a dosage form that is an encapsulated gastric retention vehicle comprising specific components having adhered thereto a reservoir of a therapeutic agent. Moreover, the dosage form must further meet functional limitations recited in the claim. Applicants respectfully submit that Curatolo '443 does not suggest let alone teach an encapsulated bonded combination of a gastric retention vehicle and bonded reservoir. Accordingly, Applicants respectfully submit that the rejection of claim 67 should be withdrawn.

[19] Turning now to claims 68 - 77, these claims depend from claim 67. Because claim 67 is not anticipated, claims 68 - 77 depending therefrom are not anticipated. Accordingly, Applicants respectfully submit that the rejection of claim 68 - 77 should be withdrawn.

[20] Turning now to claim 78, claim 78 describes with particularity a dosage form that includes first and second compacted compositions at least one of which bears a water-activated adhesive. Curatolo '443 does not suggest let alone teach anything remotely similar to the inventive dosage form of Applicants' claim 78. The Office has not pointed to any teaching anywhere in Curatolo '443 of *any* of the limitations of claim 78. Accordingly,

Applicants respectfully submit that the rejection of claim 78 should be withdrawn.

[21] Turning now to claim 79, claim 79 describes with particularity a multilayered dosage form. Curatolo '443 does not each a multilayered dosage form, let alone most if not all other elements (limitations) of claim 79. Accordingly, Applicants respectfully submit that the rejection of claim 79 and claims 80 - 82 depending therefrom should be withdrawn.

[22] Claims 83 – 85 and 99 – 101 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Patrick S. –L. Wong et al., United States Patent 6,342,249 (Wong '249). Because Wong '249 does not teach all of the elements (limitations) of Applicants' claims, arranged as Applicants have arranged them, Applicants respectfully traverse.

[23] Wong '249 discloses a dosage form that comprises a wall structure that, in each aspect of the invention of which Applicants are aware, has at least one exit orifice [3:33 – 6:10], a push (expandable) layer, and a drug layer having contained therein a plurality of particles in which the liquid, active agent has been sorbed [8:51 – 55]. In some aspects, the push layer can be omitted (Figure 2), but this would defeat what Applicants understand to be the principle of operation of the dosage form of Wang '249. Wang does not suggest, let alone teach, that the drug layer or push layer should contain tannic acid, as required by Applicants' claims 83-85.

[24] Because Wong '249 does not teach all of the elements of Applicants' claims, Wong '249 cannot be said to anticipate claim 83, or claims 84 & 85 that depend therefrom and add limitations thereto. Accordingly, Applicants respectfully submit that the rejection of claims 83 – 85 should be withdrawn.

[25] Turning now to claim 99 – 101, these claims are cancelled, rendering this rejection moot.

[26] Claims 102 – 104 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by David Swanson and David Edgren, United States Patent 4,326,525 (Swanson '525). Because Swanson '525 does not suggest, let alone teach, all of the elements (limitations) of Applicants' claims 102 -104, arranged as Applicants have arranged them, Applicants respectfully traverse.

[27] Swanson '525 teaches an osmotic device (dosage form) that can be used to administer a drug, for example methylphenidate. The osmotic device can include tannic acid. The device of Swanson '525 provides a zero-order release rate [7:26 – 29]. Swanson '525 does not suggest, let alone teach, a dosage form that provides for sequential , time-separated (*ca.* 3 – 5 hr.) dosage of methylphenidate, as required by Applicants' claim 102 and claims 103 and 104 that depend from claim 102. Also, Applicants respectfully submit that Swanson

'525 does not suggest the express limitation that both sequential releases be in the patient's stomach. Applicants respectfully submit that the rejection should be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

[28] Claims 8, 15 – 18, and 39 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Curatolo '443. Because Curatolo '443 does not suggest all of the limitations of Applicants' claims 8, 15 – 18, and 39, Applicants respectfully traverse.

[29] According to Applicants' best understanding of the rejection, the Office bases the rejection on the fact that, although Curatolo '443 does not teach the express ratios of excipients recited in claim 8, the ratios are, it is alleged, merely design choices or the product of routine optimization. Applicants respectfully submit that, in doing so, the Office overlooks other differences between the claimed invention, as a whole, and the prior art.

[30] Applicants' claim 8 depends from claim 1, and *per force*, includes the limitation that the gastric retention vehicle composition expands about 3 fold in about 15 minutes of contacting gastric fluid. Applicants respectfully submit that Curatolo '443 provides no guidance at all on, and the Office has not pointed to anything in the ken of the skilled artisan relating to, the particular combination of cellulose derivatives that would produce the particular desired swelling rate (three fold in about 15 min.) that applicants were first to discover accrues to the combination recited in claim 8 (and others).

[31] Applicants respectfully submit that nothing in Curatolo '443 or in the knowledge in the art teaches or suggests a gastric retention vehicle that comprises a hydrogel itself comprised of hydroxypropyl methylcellulose and hydroxypropyl cellulose in a ratio of about 1:3 to about 5:3 wherein the volume of the composition increases about threefold in about 15 minutes of contacting gastric fluid. Thus, the applied art neither teaches nor suggests all of the limitations of Applicants' claim 8. Accordingly, Applicants respectfully submit that the rejection should be withdrawn. See M.P.E.P. § 2143.03.

[32] Claims 86 – 89 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Wong '249 because, it is alleged, claims 86 -89 merely recite optimum or workable concentrations gleaned from routine optimization. Because the analysis applied by the Office fails to consider the claimed invention as a whole, in view of all limitations recited in the claims, Applicants respectfully traverse.

[33] Turning first to claim 86, this claim describes with particularity a pharmaceutical dosage form comprising:

10% - 14% HPMC

42% - 47% HPC
7% - 12% crosscarmellose Na
6% - 9% tannic acid
18% - 22% levodopa
3% - 6% carbidopa
optional lubricant

[34] Wong '249 teaches a dosage form having a wall with at least an exit orifice and a drug layer that has a liquid, active agent, for example levodopa, absorbed on porous particles. The porous particles can be porous crosscramellose sodium. Wong '249 does not teach or suggest any other element (limitation) of claim 86 and, at most, would motivate the skilled artisan to select other particles that are porous particles because, Applicants respectfully submit, only porous particles function in the dosage form of Wong '249. Applicants respectfully submit that the Office has failed top present argument on how Wong '249 teaches all of the limitations of Applicants' claim 86. Accordingly, Applicants respectfully submit that the rejection of claim 86 should be withdrawn.

[35] Because independent claim 86 is not obvious, claims 87 – 89 are likewise not obvious. See M.P.E.P. § 2143.03. Accordingly, Applicants respectfully submit that the rejection of claims 87 – 89 should be withdrawn.

[36] Claims 22, 34, 35, 97, 98, and 105 - 112 were rejected under 35 U.S.C. § 103(a) as allegedly obvious over Wong '249 in view of Swanson '525. Because neither Wong '249 nor Swanson '525, alone or in combination, teach or suggest all of the limitations of Applicants' claims, Applicants respectfully traverse.

[37] Turning first to independent claim 22, claim 22 describes with particularity a dosage form that, among other things, must degrade into fragments too small to cause gastric retention. Neither Wang '249 nor Swanson '525 teach or suggest this limitation. Because all of the elements (limitations) of claim 22 and, *per force*, claims 34, 35, 97, and 98 depending therefrom are not taught or suggested in the art applied, Applicants respectfully submit that the rejection should be withdrawn.

[38] Turning now to claims 105 - 107, claims 105 - 107 depend from claim 102 and, accordingly are limited to a method of treating e.g. ADD by administering a single dosage form that releases first and second doses of methylphenidate in the stomach, such that the first a second doses are released 3 - 5 hours apart. Claim 105 further limits the dosage form used in the method to a homogeneous matrix that includes a hydrogel, a superdisintegrant, and tannic acid, wherein the methylphenidtae is in particles, at least a portion of which particles have a timed-release coating. Nothing in Wong '249 or Swanson '525 teaches or suggests this limitation. To the extent that either Wong '249 or Swanson '525 teaches

sequential (i.e. pulsed") dosage 3 - 5 hours apart, absent the invite gastric retention features of the instant invention, these sequential doses would not both be in the stomach as required by applicants claims.

[39] Claim 106 requires a reservoir with a delayed-release coating. Neither Wong '249 nor Swanson '525 teach or suggest this limitation. Concerning claim 107, claim 107 requires a gastric retention vehicle within a capsule wherein the gastric retention vehicle has both a reservoir and a coating of methylphenidate. Because neither Wong '249 nor Swanson '525, alone or in combination, teach or suggest all of the elements of Applicants' claims 105 - 107, Applicants respectfully submit that the rejection should be withdrawn.

[40] Turning now to claims 108 - 112, claim 108 describes with particularity a process for making a pharmaceutical product. The entire pharmaceutical product that is made by the method expands rapidly upon contacting gastric fluid.

[41] Wong '249 discloses a dosage form for liquid active agents having an expandable layer. According to Applicants' best understanding of Wong '249, this expandable layer does not itself include a therapeutic agent and functions to force or "pump" drug-containing fluid or particles out of the dosage form. Wong '249 does not teach or suggest a method for making a pharmaceutical product by combining a superdisintegrant, tannic acid, and a therapeutic agent such that the entire pharmaceutical product expands rapidly upon contacting gastric fluid.

[42] Nothing in Swanson '525 would suggest modifying the dosage form of Wong '249 to disperse the therapeutic agent throughout the dosage form, as Applicants do, and to cause the entire dosage form of Wong '249, not just a layer within, to expand. Indeed, Applicants respectfully submit that such modifications of Wong '249 are wholly inconsistent with the principle of operation of the dosage form of Wong '249.

[43] Because neither Wong '249 nor Swanson '525, alone or in combination, teach or suggest all of the limitations of Applicants' claim 108, Applicants respectfully submit that the rejection should be withdrawn.

[44] Turning now to claims 109 - 112, which depend from claim 108. Because claim 108 is not obvious claims 109 - 112 are also not obvious.

Claim Rejections Under 35 U.S.C. § 112

[45] Clams 88 and 97 were rejected under 35 U.S.C. § 112 as allegedly indefinite.

[46] The Office asserts that the word "averting" in claim 97 is unclear. Applicants respectfully submit that, when read as part of the phrase "averting or treating", the word

"averting" would denote to the skilled artisan the concept of preventing or prophylaxis. Applicants respectfully submit that the skilled artisan would be well aware of the meets and bounds of claim 97 and that the rejection should be withdrawn.

[47] Concerning claim 88, Applicants regret that they may not fully comprehend the nature of the rejection. The dosage form of claim 88 has two structural elements: a reservoir and a shell. applicants respectfully submit that the comma before "embedded" make it clear that the clause following refers to the just-described reservoir.

Conclusion

[48] Based on the forgoing amendments and remarks, Applicants respectfully submit that the claims are now in condition for allowance, which allowance is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would advance prosecution of the application, the Examiner is invited to call the undersigned attorney.

[49] A petition for extension of time with an authorization to debit the petition or other fees Deposit Account 11-0600 is filed herewith.

Respectfully submitted,

Date: 31 Mar. '05

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